

REMARKS

By this Amendment, Applicants propose to amend claims 1, 12, 36, 40, 44, and 48-50 to recite that the second enzyme has reduced exonuclease activity. Support for the amendment to the claims comes from the specification, as originally filed, at page 20, lines 17-19, and page 49, line 26 through page 50 (Table 1). Applicants note that the cited disclosure on page 20 discusses "preferable" mutants; however, it is well settled law that an applicant is not required to claim only a preferred embodiment of the invention. Claims 1, 3, 10-12, 14, 20, 22-24, 26, 30, 31, and 33-51 are currently pending in the application. Claims 23, 24, 26, 30, and 33-35 stand as withdrawn from further consideration by the Office, as being drawn to a non-elected invention.

I. *Restriction Requirement*

The Office continues to withdraw claims 23, 24, 26, 30, and 33-35 as directed to a non-elected invention. (Final Office Action at page 2.) Applicants note for the record that the non-elected claims are directed to methods of using the enzyme mixtures of the elected claims. As such, upon a finding of allowability of the elected claims, and in particular claim 1, the withdrawn claims should be re-joined and examined in this application.

II. *Rejections Under 35 U.S.C. § 103*

The Office rejects claims 1, 3, 10-12, 14, 20, 22, 36, 37, 40, 41, 44, 45, and 48-51 under 35 U.S.C. § 103(a) as unpatentable over U.S. Patent No. 5,436,149 to Barnes et al. ("*Barnes*"), U.S. Patent No. 6,183,997 to Hogrefe et al. ("*Hogrefe*"), and U.S.

Patent No. 6,881,559 to Sobek et al. ("*Sobek*"). (Final Office Action at pages 2-8.) The Office relies on *Barnes* for the teaching of a mixture containing a DNA polymerase lacking 3'-exonuclease activity and a DNA polymerase exhibiting 3'-exonuclease activity. The Office relies on *Sobek* for the teaching of a Family B-type DNA polymerase having a mutation at the Y-GG/A motif. The Office relies on *Hogrefe* for the teaching of compositions that contain a DNA polymerase and a polymerase enhancing factor. Applicants traverse this rejection and submit that the claims, as amended herein, are not rendered obvious by the combination of cited references.

Applicants will discuss the rejection as it applies to independent claims 1, 12, 36, 40, 44, 48, 49, and 50, with the understanding that the comments are equally applicable to their respective dependent claims.

It is well established law that, in order to set forth a *prima facie* case of obviousness, the reference(s) relied upon must teach or suggest each and every limitation of the claim at issue. Applicants have already discussed the disclosure of *Barnes* as it relates to the three mutants made by *Barnes* and their characterization with respect to DNA polymerization activity and exonuclease activity. See Applicants response of 5 January 2010. In that response, Applicants argued that *Barnes* does not disclose a mutant polymerase having reduced 5'-3' DNA polymerase activity as compared to the wild-type enzyme from which it is derived. In the Final Office Action, the Office identifies claim 8 as a disclosure that teaches the use of a mutant Pfu polymerase having reduced 5'-3' DNA polymerase activity. Although Applicants have reviewed *Barnes* in detail again, they have been unable to find written description or enabling support for claim 8 of *Barnes*. As such, Applicants submit that *Barnes* is not

an enabling disclosure for the subject matter relied upon by the Office, and thus is not suitable prior art for rejecting the present claims.

Although Applicants believe that *Barnes* is not competent prior art, in an effort to expedite allowance of this application, by this Amendment, Applicants propose to amend the independent claims to recite that the second polymerase (*i.e.*, the mutant Pfu enzyme of *Barnes*' claim 8) has reduced 3'-5' exonuclease activity as compared to the wild-type enzyme from which it is derived. Applicants submit that *Barnes* does not disclose such an enzyme.

Furthermore, the use of such an enzyme in the system of *Barnes* would not be obvious because the "second enzyme" of *Barnes* is present specifically for its exonuclease activity. Throughout *Barnes*, it is emphasized that the key feature of the invention is the combination of a relatively high amount of a DNA polymerase having high polymerase activity with a relatively low amount of a DNA polymerase having high exonuclease (*i.e.*, proofreading) activity. In the system of *Barnes*, the combination allows for a high yield of long nucleic acid products. The high level of the first polymerase (with high DNA polymerase activity) provides the ability to achieve a high yield and long product, while the low level of the second enzyme (with exonuclease activity) provides the ability to correct errors, which is necessary to allow the first enzyme to perform its intended function. As such, the second polymerase should have as high of an exonuclease activity as possible. Lowering the exonuclease activity would reduce the overall performance of the system of *Barnes* and thus would not be an obvious alteration to make.

If a proposed modification to a reference would render that reference unsuitable for its intended purpose, there is no motivation to make such a modification. See MPEP § 2143.01 V. and § 2145 X.D. In the present situation, in order to set forth a *prima facie* case of obviousness, the Office must modify the second polymerase (*i.e.*, the mutant Pfu polymerase of claim 8) to have reduced 3'-5' exonuclease activity. Doing so would render the polymerase blend of *Barnes* unsuitable for its intended purpose. As such, neither *Barnes* nor the other two references relied upon by the Office provide a suggestion or motivation to modify *Barnes* as necessary for the teachings of the combination of references to arrive at the presently claimed invention.

Applicants submit that, for at least the reasons set forth above, the combination of *Barnes*, *Sobek*, and *Hogrefe* does not render the claimed invention, as amended herein, obvious. Therefore, Applicants request that the Office reconsider and withdraw the rejection of claims 1, 3, 10-12, 14, 20, 22, 36, 37, 40, 41, 44, 45, and 48-51 as unpatentable under 35 U.S.C. § 103(a).

III. *Double Patenting*

The Office provisionally rejects claims 1, 3, 10-12, 14, 20, 22, and 36-51 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 2, 5-8, 22, 27, 31, and 40-44, of co-pending Application No. 10/702, 400. (Final Office Action at page 9.) Applicants acknowledge this provisional rejection and request that the Office hold the rejection in abeyance until one or the other application is in condition for allowance. At that time, Applicants will take appropriate action.

IV. *Conclusion*

In view of the foregoing amendments and remarks, Applicants respectfully request entry of this Amendment, reconsideration and reexamination of this application, and the timely allowance of the pending claims. This is believed to be a complete and proper response to the Final Office Action.

Please grant any extensions of time required to enter this response and charge any required fees to Deposit Account No. 50-2961.

Respectfully submitted,
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